3. RESPONSE/REMARKS

3.1 STATUS OF THE CLAIMS:

Claims 1-9, 11-16 and 19-24 were pending at the time of the Action.

Claims 19 and 22 have been canceled without prejudice or disclaimer.

Claims 1, 13, 14 and 24 have been amended herein.

Claims 25-29 have been added herein.

Claims 1-9, 11-16, 20, 21 and 23-29 remain pending in the case.

Applicants appreciate the finding by the Examiner that all pending claims possess utility, are definite, and free of the prior art. Applicants request that the Examiner rejoin the species illustrated in currently withdrawn claims 4-5 and 15-16 in view of an allowable generic linking claim.

3.2 A SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IS PROVIDED

Applicants' representative encloses herewith a Supplemental IDS, along with the required fee, making additional references of record in the pending Application. Consideration of these references by the Examiner is earnestly solicited.

3.3 THE OBJECTION TO CLAIMS 13 AND 14 IS OVERCOME.

The Action at page 2 objected to claims 13 and 14 allegedly as being unclear.

Applicants respectfully traverse. However, in order to facilitate conclusion of prosecution on the merits of the instant application, Applicants have complied with the Examiner's request, and have introduced the appropriate chemical structures of the claimed compounds as recited in claims 13 and 14. Applicants have also introduced the structures recited

in claims 13 and 14 into the relevant section of the specification at page 20 by the accompanying amendment. No new matter is introduced, however, as the enumerated structural formulae represent compounds that were set forth in the priority application (PCT/AU02/01427), which was previously incorporated by reference in its entirety into the present application (see *e.g.*, Specification at page 2, lines 23-25, and page 13, lines 26-31).

Applicants believe this fully addresses the Office's concerns, and respectfully requests that the objection now be withdrawn.

3.4 THE REJECTIONS UNDER 35 U. S. C. §112, 1ST PARAGRAPH, ARE OVERCOME.

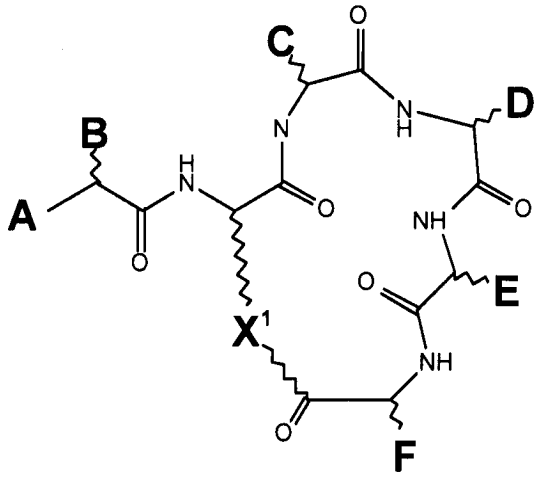
The Action at pages 3-6 rejected claims 1-9, 11-16 and 19-24 under 35 U. S. C. § 112, 1st paragraph, allegedly as lacking enablement. The Action considers that the Specification, "while being enabling for antagonists of C5a receptor for the claimed treatment of inflammatory bowel disease, does not reasonably provide enablement for any antagonist represented by formula 1 having agonist activity."

The Action at pages 6-10 further rejected claims 1-9, 11-16 and 19-24 under 35 U. S. C. § 112, 1st paragraph, allegedly as lacking enablement. The Action considers that the Specification, "while being enabling for methods to treat ulcerative colitis, does not reasonably provide enablement for the treatment of any and all diseases encompassed by "inflammatory bowel disease.""

As to each of these rejections, Applicants respectfully traverse.

However, in order to address the concern raised by the Examiner, Applicants have clarified the language of claim 1 to delete the limitation that the compounds "have substantially no agonist activity." Applicants believe this clarification overcomes the present rejection.

Moreover, based upon the helpful remarks by the Examiner in the Action, Applicants have added new claims 25-29 directed to methods acknowledged by the Office to be patentable, *i.e.*, a method for treating or ameliorating the symptoms of inflammatory bowel disease using a C5a receptor antagonist compound that comprises a cyclic peptide or peptidomimetic compound of formula I:



where **A** is H, alkyl, aryl, NH_2, NH-alkyl, $N(alkyl)_2$, NH-aryl, NH-acyl, NH-benzoyl, $NHSO_3$, $NHSO_2$-alkyl, $NHSO_2$-aryl, OH, O-alkyl, or O-aryl;

B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

C is the side chain of a D-, L- or homo-amino acid, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is not the side chain of glycine or D-alanine, a bulky planar side chain, or a bulky charged side chain;

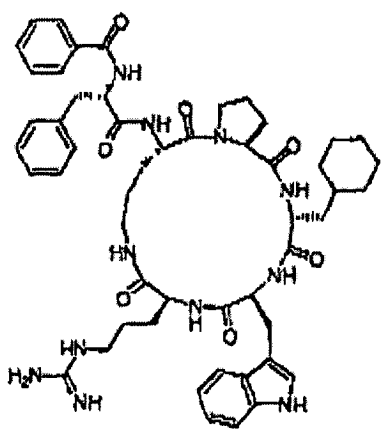
E is a bulky substituent, but is not the side chain of D-tryptophan, L-*N*-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine; and

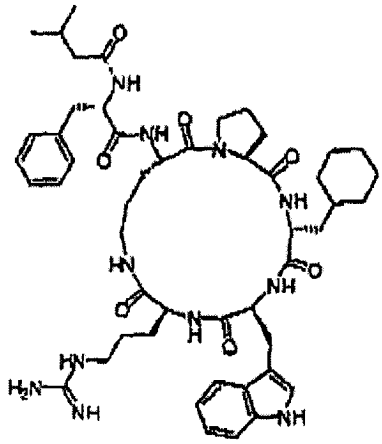
X is $-(CH_2)_nNH-$ or $(CH_2)_n-S-$, where n is an integer of from 1 to 4; $-(CH_2)_2O-$; $-(CH_2)_3O-$; $-(CH_2)_3-$; $-(CH_2)_4-$; $-CH_2COCHRNH-$; or $-CH_2CHCOCHRNH-$, where R is the side chain of any common or uncommon amino acid, and particularly compounds such as PMX53 (AcF-[OPdChaWR].

Claims 26 and 27 are respectively drawn to methods for (1) ameliorating one or more symptoms of, and (2) treating an inflammatory bowel disease in a mammal using a C5a receptor inhibitory peptide or peptidomimetic compound disclosed in the Specification, and particularly those compounds set forth in general formula I.

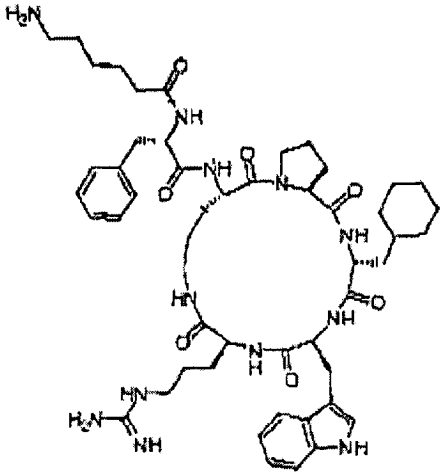
In dependent claim 28, Applicants have further specified exemplary compounds of general formula I that are useful in the methods of claim 26 and 27, namely, one or more compounds selected from the group consisting of: AcF-[OPdChaWR] (*i.e.*, compound "PMX53"),



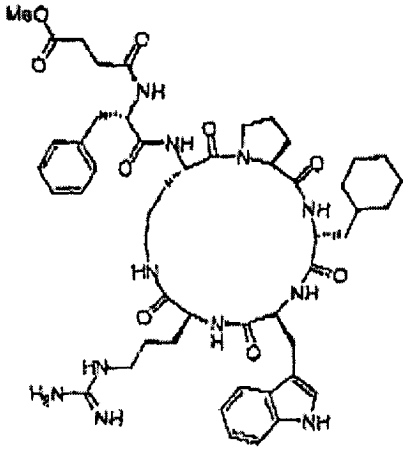
2



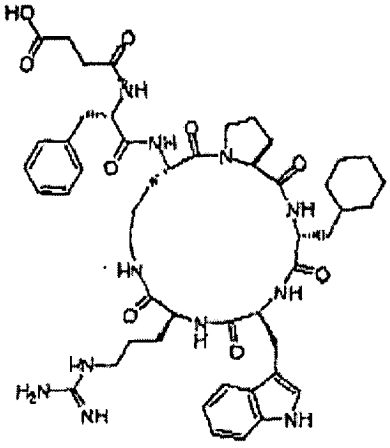
3



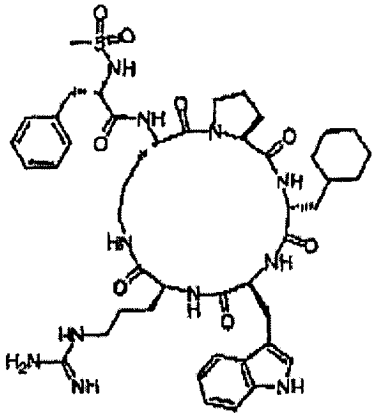
4



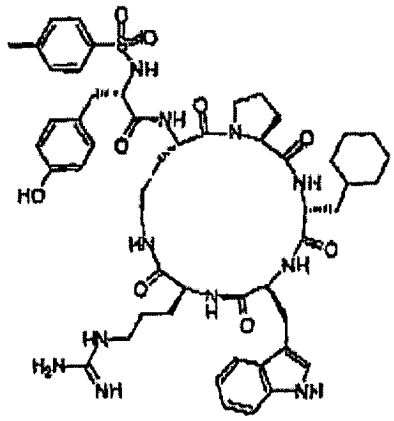
5



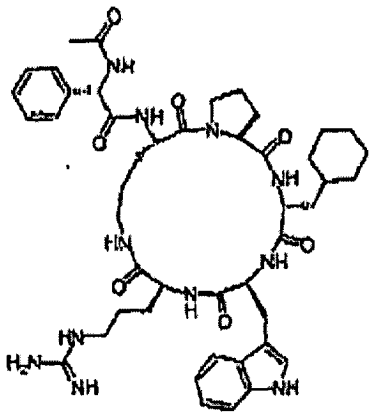
6



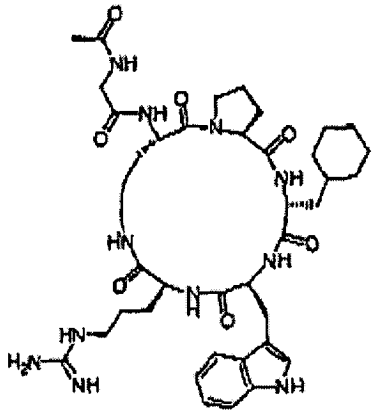
10



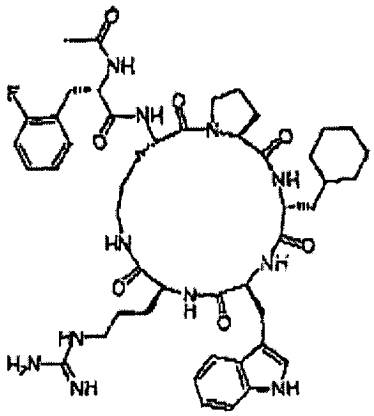
11



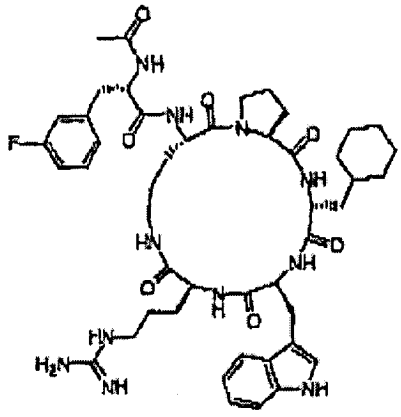
12



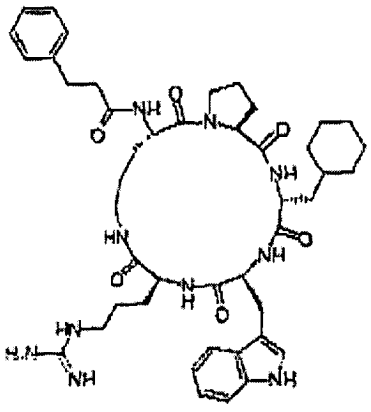
13



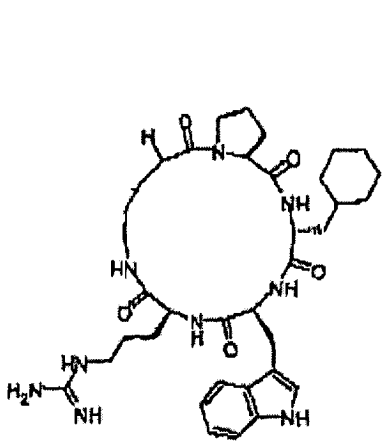
14



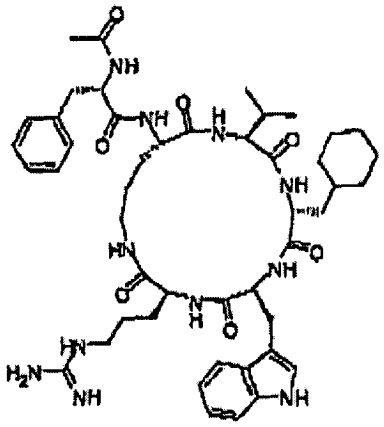
15



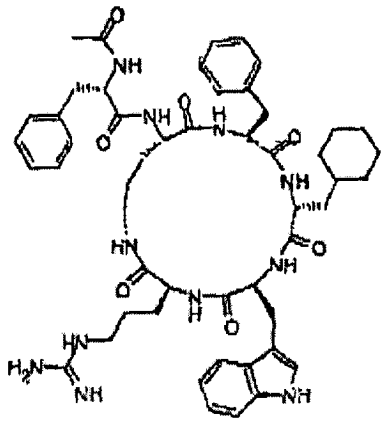
17



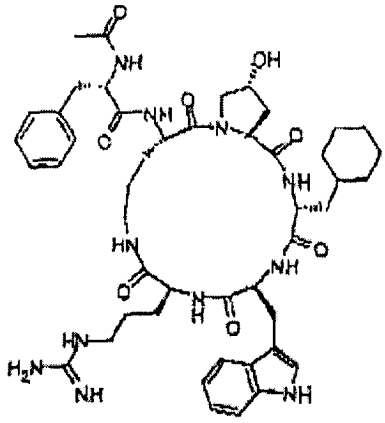
19



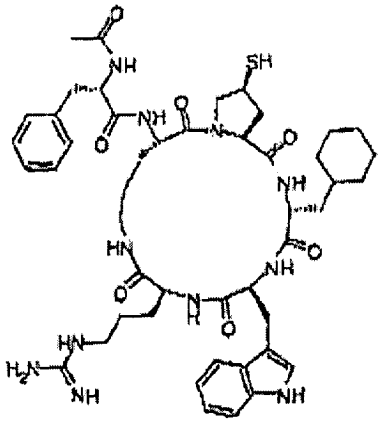
20



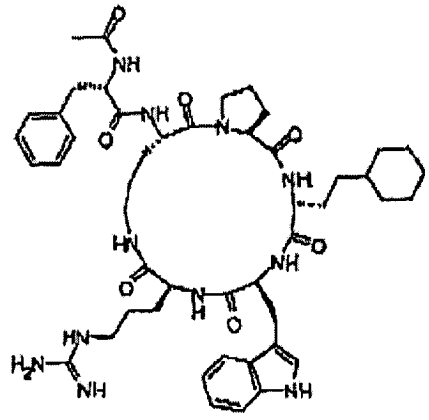
22

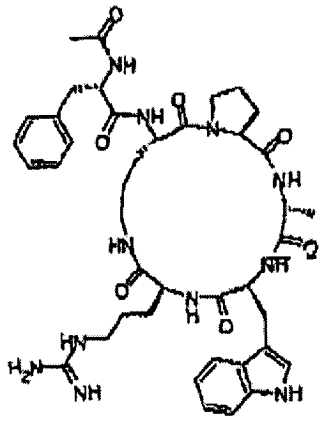


25

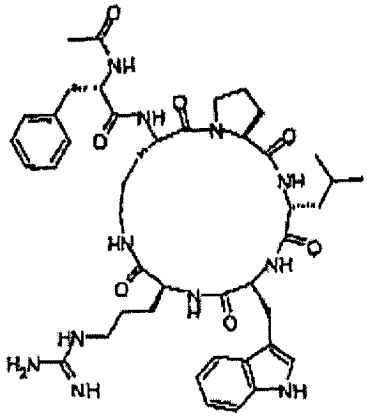


26

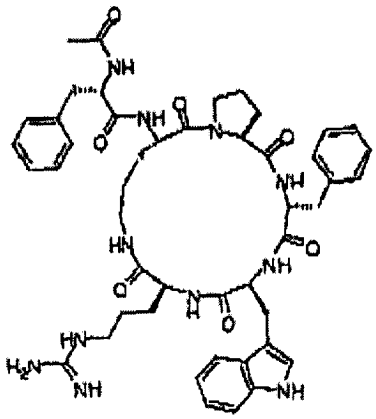




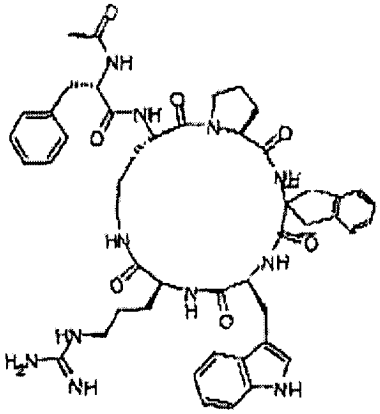
30



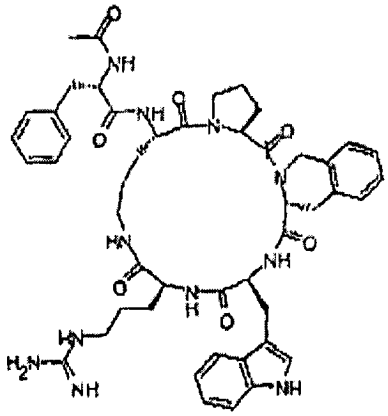
31



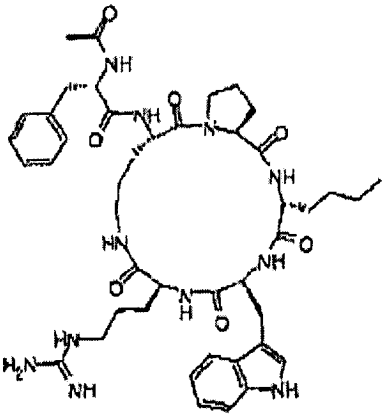
33



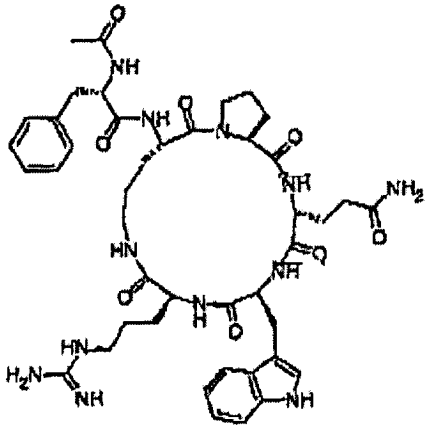
34



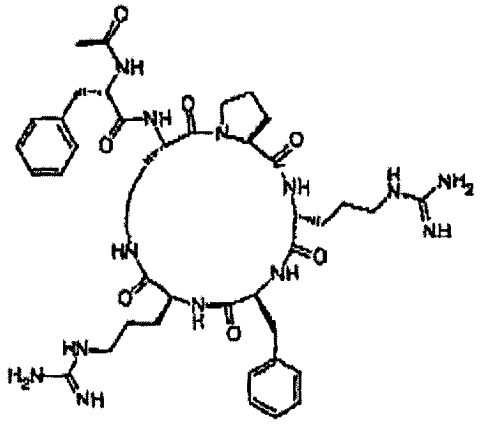
35



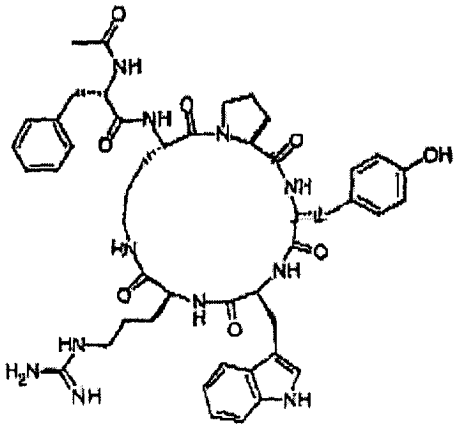
36



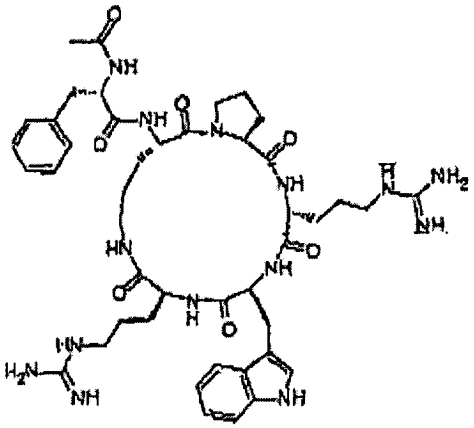
37



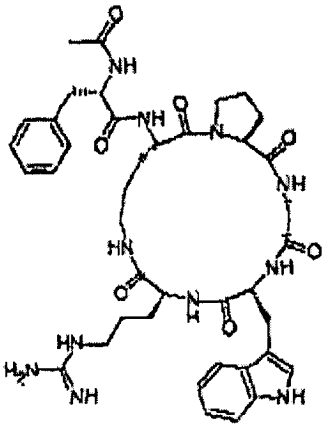
39



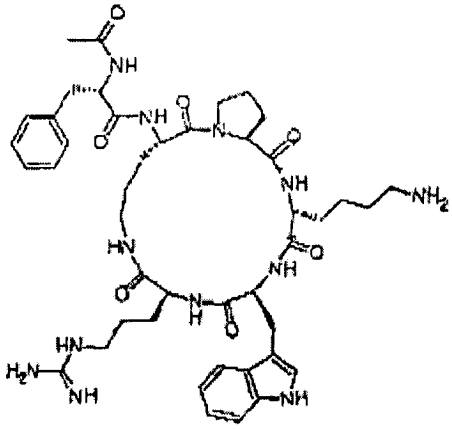
40



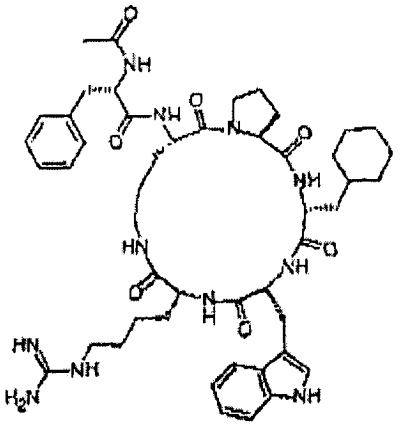
41



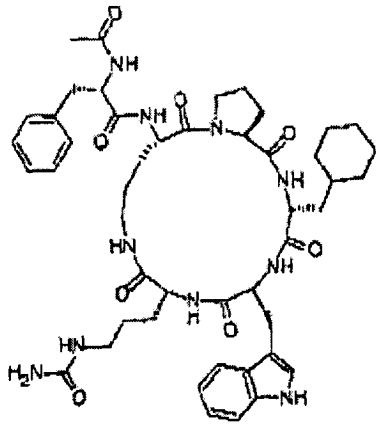
42



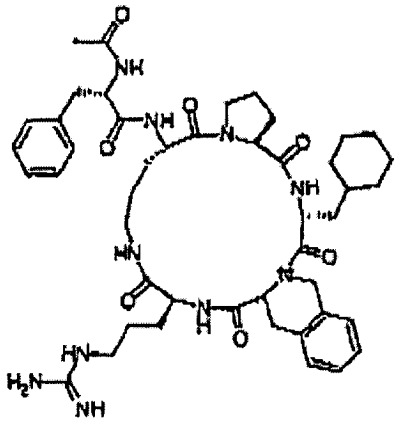
43



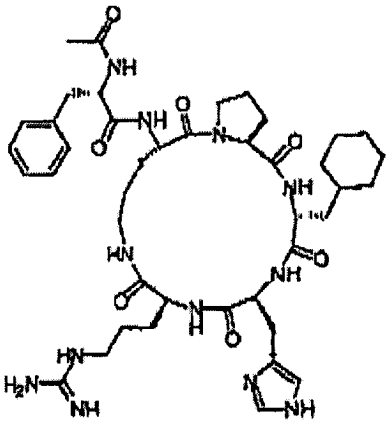
44



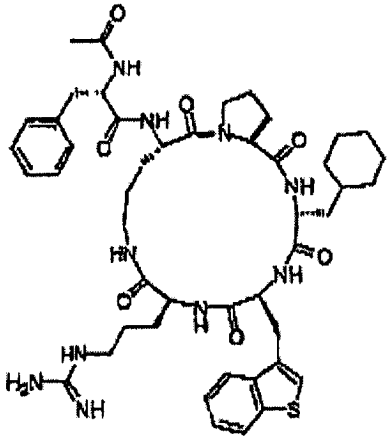
45



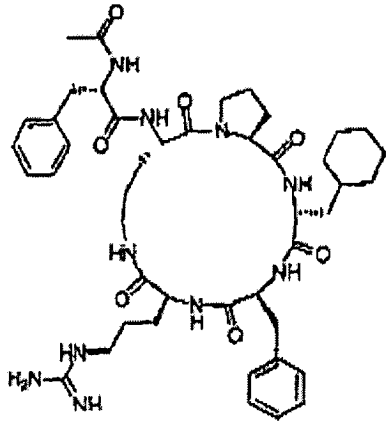
46



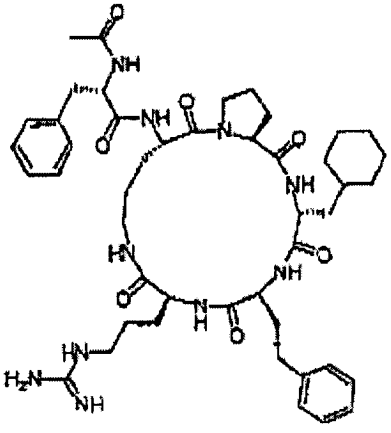
57



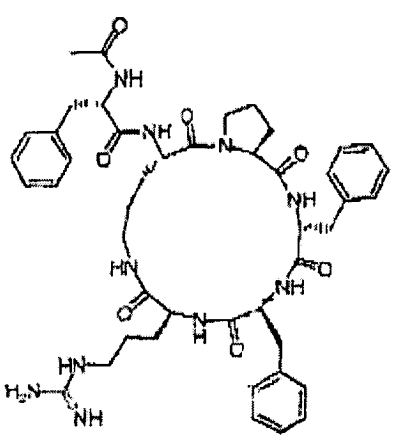
58



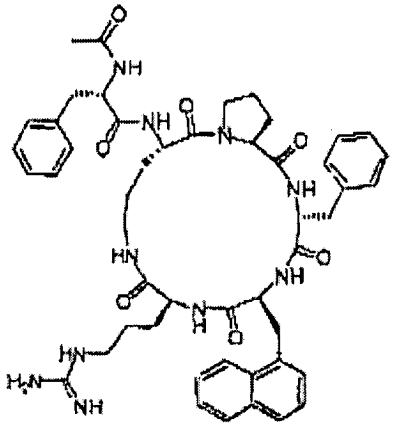
60



61

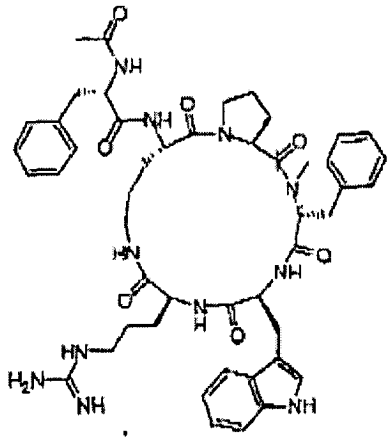


62



63

and



64

New claim 29 also recites a method for treating or ameliorating the symptoms of an inflammatory bowel disease in a mammal using one or more of the disclosed C5a receptor antagonist compounds.

Based upon the Examiner's remarks, Applicants believe that these claims are fully enabled, and are therefore allowable. Support for amelioration of symptoms is found throughout the Specification, and at least on page 10, lines 30-32.

With respect to the § 112 rejection regarding the breadth of the pending claims, the Action doubts whether the claimed methods are sufficiently enabled to allow those of ordinary skill in the art to practice the treatment of inflammatory bowel diseases in subject mammals, and humans in particular.

As is well established in the case law, the Specification need not provide exhaustive clinical data (either on animals or humans) to enable how to make and use the claimed invention. In an important case concerning rejections under 35 U. S. C. § 112, 1st paragraph, the Federal Circuit overturned the outstanding § 112, first paragraph rejections, admonishing the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *In re Brana*, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago. 34 U.S.P.Q.2d at 1439; emphasis added.

The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. In view of all the foregoing, we conclude that applicants' disclosure complies with the requirements of 35 U.S.C. § 112 ¶ 1.34 U.S.P.Q.2d at 1442-1443; citations omitted. All that is required to comply with § 112, first paragraph, is for the specification to teach how to make and use the claimed invention so that it may be practiced without undue experimentation. *In re Borkowski and Van Venrooy*, 164 USPQ 642 (C.C.P.A. 1970).

In light of the successful animal data as detailed in the specification (and acknowledged by the Examiner in the Action), the enablement rejection as applied against the pending claims is improper. With respect to the claimed methods, the Office has not provided evidence showing that one of ordinary skill in the art would reasonably doubt the direction in the specification concerning the various uses of the C5a receptor inhibitory peptide and peptidomimetic compounds of the present invention, or that the *in vivo* animal model data would not be predictive of *in vivo* results in humans. Simply stated, a sufficient *prima facie* case of deficient teaching has not been established, and the burden has not been properly shifted to the Applicants to provide rebuttal evidence.

The Action appears to be requiring the presence of a working example demonstrating clinical effectiveness *in humans* for the claimed invention. The Action appears to overlook the working animal model examples and objective teachings of the specification and instead fault the Specification for failing to provide clinical results in humans. Clearly, this is an improper standard that is not supported by the case law.

In fact, rather than requiring the presence of a working example demonstrating clinical effectiveness for each species within a claimed invention, as apparently required by the instant Action, it is well established that the specification does not even have to include any working examples. M. P. E. P. §2165.01 states this with particular clarity:

> There is no statutory requirement for the disclosure of a specific example. A patent specification is not intended nor required to be a production specification. *In re Gay*, 309 F.2d 768, 135 USPQ 311 (C.C.P.A. 1962).

All that is required to comply with § 112, first paragraph, is for the specification to teach how to make and use the claimed invention so that it may be practiced without undue

experimentation. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112, first paragraph. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ 2d 1016 (Fed. Cir. 1991). As a matter of law, it is also well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The Animal Model is Predictive of Inflammatory Bowel Diseases

The present specification provides more than adequate teaching on how to make and use the disclosed compounds in the treatment and/or amelioration of symptoms of inflammatory bowel disease. The Specification also demonstrates a credible and substantial utility for the peptide and peptidomimetic compositions both *in vitro*, and also *in vivo* in an acceptable animal model of inflammatory bowel disease.

Applicants note that the TNBS-induced animal model is widely used in the relevant art, and is the *de facto* standard animal model for inflammatory bowel diseases. (see *e.g.*, Morris *et al.*[2]) which describes the development of the animal model, and its application to inflammatory bowel diseases (a copy is attached hereto as **Exhibit A**). Moreover, Applicants note that the model has been widely used to examine the efficacy of various candidate drugs for the treatment of inflammatory bowel diseases in general (see *e.g.*, Fukunaga *et al.*[3] Dip *et al.*,[4] Toulouse *et al.*,[5] and Ikeda *et al.*,[6] attached hereto as **Exhibits B, C, D and E**, respectively).

---

[2]*Gastroenterology*, **96(3):**795-803,March 1989.
[3]*J. Gastroenterol.*, **38:**451-459, 2003.

Applicants assert therefore, that sufficient the animal model utilized is well-established in the field as a predictive and informative animal model for mammalian inflammatory bowel diseases. As such, Applicants believe that sufficient enabling methodology and *in vivo* clinical experimental animal model data have been provided by the Applicants to enable one of skill in the art to make and use the claimed methods. As such, Applicants now respectfully request that these enablement rejections be withdrawn.

3.5 CONCLUSION

Applicants believe that the present paper is fully responsive to the outstanding Action, and that the pending claims are in condition for allowance. As such, Applicants respectfully request that the withdrawn species now be rejoined and that examination on the merits be concluded. In the interest of concluding prosecution on the merits and advancing certain claims of commercial interest to ready allowance, a Notice of Allowance and Issue Fee Due is earnestly sought from the Office in response to the present submission.

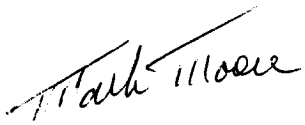
Applicants reserve their right to re-file claims to one or more aspects of the invention as originally claimed in one or more continuing application(s) retaining the priority claim of the present application.

---

[4] *J. Pharmacol. Exp. Ther.*, **302(3):**1013-1022, 2002.
[5] *Brit. J. Pharmacol.*, **129:**193-199, 2000.
[6] *Dig. Dis. Sci.*, ePrint ahead of publication, Springer, Online availability: Dec. 1, 2007.

Should any issues remain outstanding upon consideration of the present paper and entry of the foregoing amendment, or should the Examiner have any questions or concerns, a telephone call to the undersigned Applicants' representative at the Examiner's convenience *prior to the issuance of any subsequent Official Action* would be sincerely appreciated.

Respectfully submitted,

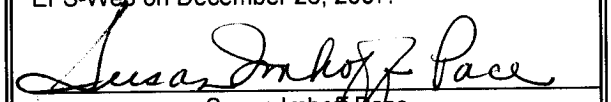


Mark D. Moore, Ph.D.
Registration No. 42,903

Date: December 26, 2007
HAYNES AND BOONE, LLP
901 Main Street, Suite 3100
Dallas, Texas 75202-3789
Telephone: 713-547-2040
Facsimile: 214 200-0853
36672.7
H:708607_1

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office *via* EFS-Web on December 26, 2007.



Susan Imhoff Pace